

**REMARKS**

Entry of this amendment is requested.

It is believed that the objections to claims have been overcome by the amendments to the claims.

Claims 3 and 1-2, 4-5, 8-9 and 18-20 (in part) were provisionally rejected on the ground of nonstatutory obviousness-type double patenting for allegedly being unpatentable over claims 1-3, 5 and 9-18 of co-pending application no. 10/399,051 in view of Hatzelmann and Schudt ("Hatzelmann"). Applicants respectfully traverse.

Hatzelmann discloses a comparison of roflumilast, a phosphodiesterase-4 (PDE-4) inhibitor, and its N-oxide pyridine derivative. In this context, it is stated on page 277, first paragraph of the Discussion, "roflumilast is a potent and selective PDE-4 inhibitor with anti-inflammatory and immunomodulatory action *in vitro*. These features also translate to the main metabolite (N-oxide) of roflumilast formed *in vivo*; it is therefore likely that the N-oxide contributes to the overall action of roflumilast in animal species as well as humans."

However, the chemical structure of roflumilast and its N-oxide differ remarkably from the chemical structure of the 7-azaindoles according to the present invention. Therefore, it is respectfully submitted that it would be obvious to a person of ordinary skill in the art that N-(pyridine-4yl)-7-azaindole-3-yl-glyoxyamides disclosed in copending U.S. 10/399,051 and their corresponding N-oxide pyridine derivatives would show similar activity with respect to their function as PDE-4 inhibitors. In support of this, Applicants invite the Examiner to review Hulme et al. (Bioorganic and Medicinal Chemistry Letters (1998), 8, 3053-3058) which is cited in an accompanying IDS and discloses the synthesis and *in vitro* and *in vivo* evaluation of several orally active indole-N-oxide PDE-4 inhibitors. In this context, the Examiner's attention should be drawn to Table 1 which shows different N-oxide pyridine derivatives to be remarkably less active than the corresponding parent compounds (cf. compounds 8/9 and compounds 13/14).



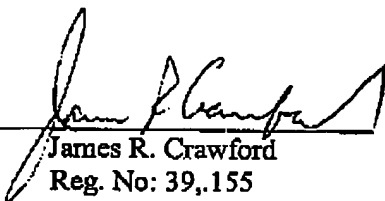
In summary, the objection raised by the Examiner is based on inadmissible hindsight, as it is respectfully submitted that it would not be obvious for a person of ordinary skill in the art to look at the PDE-4 inhibitors disclosed in the claims of the co-pending application U.S. 10/399,051 and to expect the N-oxide pyridine derivatives according to the present application to inhibit PDE-4 with similar efficiency, even in view of the Hatzelmann reference, given the teaching of Hulme et al.

In view of the foregoing, allowance is respectfully requested.

The Commissioner is hereby authorized to charge any deficiency in the fees filed to our Deposit Account No. 50-0624, under Order No. NY-HUBR 1261-US.

Respectfully submitted

FULBRIGHT & JAWORSKI L.L.P.

By   
James R. Crawford  
Reg. No: 39,155

666 Fifth Avenue  
New York, New York 10103  
(212) 318-3148  
Enclosure